This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

15

5

THE USE OF AN AQUEOUS SOLUTION IN THE PREPARATION OF A MEDICAMENT FOR USE IN THE TREATMENT OF LIVE ANIMALS

Field of the Invention:

This invention relates to the use of an aqueous solution in the preparation of a medicament for use in the treatment of live animals.

Background to the Invention:

For the purposes of this specification, the term "animal" should be construed to include within its meaning sheep, cattle, goats, pigs, chickens, ostriches, reptiles and the like; the term "disease" should be construed to include within its meaning diarrhoea; the term pathogen should be construed to include within its meaning micro-organisms such as E-coli; and the term "medicament" should be construed to include within its meaning oral bactericides and bactericidal inhalants. The Applicant envisages that the invention will be applicable particularly, but not exclusively, in the preparation of a medicament for use in the treatment of pathogenic micro-organisms in weaner piglets and chicklets.

The presence of antibiotic residues in food products lead to allergic and anaphylactic reactions in humans. The development of resistant strains of micro-organisms makes anti-microbials ineffective.

Object of the Invention:

It is accordingly an object of the invention to provide inexpensive, novel and alternative anti-microbials that overcome the above disadvantages.

In accordance with a first aspect of the invention, there is provided the use of a composition in the preparation of a medicament for use in the treatment of pathogenic micro-organisms in a live animal, the composition comprising an electro-chemically activated anion-containing aqueous solution.

- In accordance with a second aspect of the invention there is provided a composition in the preparation of a medicament for the treatment of pathogenic micro-organisms in live animals, the composition comprising an electro-chemically activated anion-containing aqueous solution, the composition substantially as herein defined.
- In accordance with a third aspect of the invention there is provided a method of treating pathogenic micro-organisms in a live animal, the method including the step of administering a dosage of a composition comprising an electro-chemically activated anion-containing aqueous solution to the animal, the anion-containing aqueous solution being substantially as herein defined.
- The anion-containing aqueous solution may be prepared by means of electrolysis of an aqueous solution of a salt. The salt may be sodium chloride.

 In particular, it may be non-iodated sodium chloride or potassium chloride.

15

5

WO 99/20287 PCT/US98/22372

The anion-containing solution and the associated cation-containing solution may be produced by an electro-chemical reactor or so-called electrolysis device.

The electro-chemical reactor may include a through flow, electro-chemical cell having two co-axial cylindrical electrodes with a co-axial diaphragm between the electrodes so as to separate an annular inter electrode space into a catalytic and an analytic chamber.

The anion-containing solution is referred to hereinafter for brevity as the "anolyte solution" and the cation-containing solution is referred to hereinafter for brevity as the "catholyte solution".

The anolyte solution may be produced from an aqueous NaCl solution, electrolysed to produce radical cation and radical anion species, the anolyte solution having a redox potential up to about + 600 mV to + 800 mV. These species may be labile and after about 96 hours, the various radical species may disappear with no residues being produced.

The anolyte solution may have a pH of about 6,5 to 7,5. The anolyte solution may include species such as ClO; ClO; HClO; OH; HO_2 ; H_2O_2 ; O_3 ; $S_2O_8^{2-}$ and $Cl_2O_6^{2-}$.

15

WO 99/20287 PCT/US98/2237

These species have been found to have a synergistic anti-bacterial and/or antiviral effect which is generally stronger than that of chemical bactericides and has been found to be particularly effective against viral organisms and spore and cyst forming bacteria.

The redox potential of the anolyte solution may be monitored during the process so that the treatment process may be monitored and controlled on a continuous basis.

The catholyte solution generally may have a pH of up to about 12-13 and a redox potential of about -980 mV. The catholyte solution may include species such as NaOH; KOH; $CA(OH)_2$; $Mg(OH)_2$; HO^- ; $H_3O_2^-$; HO_2^- ; $H_2O_2^-$; O_2^- ; O_2^- ; O_2^- ; O_2^- .

The method of treatment may include administering the anolyte solution by soaking, rinsing or dipping the animal in the anolyte solution, applying the anolyte solution as an inhalant via an atomising or fogging process or administering the anolyte solution orally. The soaking, rinsing or dipping process is suitable for animals which can be handled with relative ease.

The processes of atomising or fogging and oral administration by addition to drinking water are both suitable for animals such as weaner piglets and

5

WO 99/20287 PCT/US98/22372

chicklets which are susceptible to stress and accompanying weight loss. The atomising or fogging process may include the step of atomising the solution into the atmosphere in a volume to be treated, forming droplets of between 5 and 100 micrometre. The method may include the preliminary step of enclosing the volume to be treated prior to atomising or fogging the enclosed volume.

The atomising or fogging process is preferably conducted at pre-determined intervals so as to maintain a suitable level of anolyte concentration in the atmosphere, thus utilising the optimum microcidal and other properties of the anolyte solution in accordance with the required administration rate.

The anolyte solution may also be applied by an atomising process in air ducting systems to destroy air-borne micro-organisms and to destroy micro-organisms present in the airways and lung tissue by inhalation.

The treatment of the animal as described above may be conducted so as to improve the weight gain as a result of the anti-microbial action of the anolyte solution.

The oxidising-free radicals present in the anolyte solution may act synergistically at a bacterial cellular level.

WO 99/20287 PCT/US98/22372

The anolyte solution may have a specific anion concentration and distribution and a redox potential in accordance with the specific application.

The pathogenic micro-organisms to be treated may include enteric pathogenic micro-organisms and respiratory pathogenic micro-organisms.

5 <u>Detailed Description of the Invention</u>:

A preferred embodiment of the invention will now be described with reference to the accompanying experiments.

In a series of experiments, the bactericidal effect of the anolyte solution was tested on animals. The results are reflected in the tables below.

An electro-chemical reactor, including a through flow, electro-chemical cell having two co-axial cylindrical electrodes with a co-axial diaphragm between them so as to separate an annular inter-electrode space into a catalytic and an analytic chamber, was used to produce anolyte and catholyte solutions.

Experiment 1 - Weaner Piglets

The anolyte solution was added to the drinking water of the weaner piglets over a period of 14 days and the results were measured in terms of average

10

15

WO 99/20287 PCT/US98/22372

weight after the 14 day period. The average weight of the administered groups were compared with the average weight of the unadministered groups.

The administered groups showed relative weight gain relative to the unadministered groups. The relative weight gains of the administered groups are reflected in Table 1 below.

Experiment 2 - Broilers (Chicklets)

Day old broilers were administered with anolyte solution (10% diluted) by addition to drinking water for 7 days. (Group C3 - 12 000 chicklets). No antibiotic medication was administered during that time. Untreated control groups (C1, C2, C4 and C5 = total 48 000 chicklets) received normal drinking water during that time. The untreated groups were routinely medicated with Tylosin for 3 consecutive days.

Bacterial analyses of the drinking water of all groups were regularly conducted during the first 7 days. Other measurements included daily mortalities and morbidities throughout and pH and ORP determinations of the drinking water during the first 7 days. All results are reflected in Table 2 below.

Medication of drinking water with anolyte solution supplied to day-old

10

15

WO 99/20287 PCT/US98/2237

chicklets for the first period resulted in a significant reduction in mortalities throughout the growth and finishing period. Mortalities increased in all the groups from the 4th week onwards mainly due to respiratory disease. It is envisaged that these could be reduced by fogging the environment with anolyte solution to eliminate airborne respiratory pathogens by means of respiratory intake.

It has been found that the efficacy of the use of the anolyte solution in the treatment of live animals depends upon the concentration of the anions in the anolyte solution, as measured by the oxidation-reduction potential (ORP) or redox potential of the anolyte solution, the flow rate through the reactor, the exposure time, i.e. the contact time between the contaminated animal and the anolyte solution and the temperature during application. By measuring the redox potential of the anolyte solution during the treatment, for example, of a weaner piglet, the available free radical concentration can be monitored. Anolyte solution has been found to be more effective at lower than at higher temperatures.

It will be appreciated that many variations in detail are possible without departing from the scope and/or spirit of the invention as claimed in the claims hereinafter.

ART 34 AMDT

202 775 8396;

Feb-11-00 10:44AM;

Page 11/13

PCTAUS 98/22372 IPEA/US 09 DEC 1993

TABLE 1

	ž.					
	Determinant	Trial		Groups		
		RITM	R2TF	RICE	R4C	<u> </u>
Treatments	10% Anolyte in drinking water - days	13	13	o	0	
	ORP range (mV) Replemishment (days)	600-650	600-650	100-150	100-1	50
	:	2	12	1.	1. 1	
Growth Performance	No per group	16	16	16	16	
	(9/10/97) Day 0 x L Mass	8,24	6,08	7,66	6,01	
	ADG	0,133	0.212	0,185	0,148	
Trestment Courses Required	Diambea pig/group	(18%)	(12,5%)	(37,5%)	(100%))
	Respiratory symptoms pigs/group	(6,25%)	(12,5%)	(18,75%)	(100%)	,
	Cost of Treatment	R14,00	R14,00	R31,50	R126,0	D
	Cost of Treatment	R0,88	R0,88	R1.97	R741	1

AMENDED SHEET

FAX RECEIVED FEB 1 1 2000

GROUP 1600

02/11/00 FRI 11:42 [TX/RX NO 5077] 2011

PCIAS 98/22372 IPEAUS 09 DEC 1999

ŝ Ξ Ĩ = Ę Ξ = Ξ = 8 7 Ž Ξ Ξ ŝ Ξ Ē ₹ Ē 3 ğ 3 3 3 ĩ = 3 Ē ž Ξ Ē Anolyte Trial in thoilers Total situ 21 days. Aversge Control = 6.0% (66 6% mars dird than Ireated) traited = 1.6% Total after 42 days: Averge Control = 9 JG% [18.9% more diad than treakd] traited = 7.89% Average Cooded = 3.16% (81% nove died than trepted)
trepted = 2.89% Total after 2A days: Average Control - 6 57% (61% nine died than trested) Total after 31 days: Average Control = 7.39% (18% more died ikan treated) Vcaled = 5.67%

FAX RECEIVED

AMENDED SHEET

FEB 1 1 2000

GROUP 1600

02/11/00 FRI 11:42 [TX/RX NO 5077] 2012

TABLE